



Verve Therapeutics Announces 2022 Anticipated Milestones and Preclinical Data on Potential Additional Dosing Regimens for its Novel Base Editing Programs

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VERVE-101 Regulatory Submissions and First Patient Treated On-track for Second Half of 2022

ANGPTL3 Program Initiation of IND-Enabling Studies Expected in the Second Half of 2022

Preclinical Data in Non-Human Primates Demonstrate Potential to Re-Dose or Sequentially Dose Base Editing Programs

CAMBRIDGE, Mass., Jan. 10, 2022 (GLOBE NEWSWIRE) -- [Verve Therapeutics](#), Inc., (Nasdaq: VERV), a biotechnology company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, today highlighted key milestones anticipated in 2022 and announced new preclinical data in non-human primates (NHPs) on additional potential dosing regimens for its base editing programs for the treatment of atherosclerotic cardiovascular disease (ASCVD) indications.

"2021 was a year of remarkable progress across all aspects of our company, with data demonstrating robust and durable gene editing and well-tolerated safety profiles with both VERVE-101 and our ANGPTL3 base editor in NHP studies. We successfully executed our IPO and further strengthened our team with several highly talented individuals," said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve. "As we look ahead, we expect 2022 will be a transformative year, with additional data expected at scientific and medical meetings throughout the year, leading to our planned transition to a clinical-stage organization in the second half of 2022. As pioneers in the industry for the treatment of cardiovascular disease, we have the opportunity to fundamentally shift how patients with ASCVD are treated and look forward to reporting more progress in the coming months."

2022 Anticipated Milestones

Verve's lead program, VERVE-101, is designed to permanently turn off the PCSK9 gene in the liver to reduce disease-driving LDL-C. VERVE-101 is being developed initially for the treatment of patients with heterozygous familial hypercholesterolemia (HeFH), a potentially fatal genetic heart disease. [Previously reported](#) data in NHPs demonstrated that a single administration of VERVE-101 led to robust, durable editing of the PCSK9 gene. Key program milestones anticipated in 2022 include:

- Clinical trial application (CTA) and investigational new drug (IND) submissions in the second half of 2022, and
- First HeFH patient treated in a Phase 1 clinical trial in the second half of 2022.

Verve's second program is designed to permanently turn off the ANGPTL3 gene, a key regulator of cholesterol and triglyceride metabolism. Verve plans to develop this program initially for the treatment of both homozygous familial hypercholesterolemia (HoFH) and HeFH. [Previously reported](#) data have demonstrated that a single administration of Verve's ANGPTL3-targeting base editor led to potent reductions in blood ANGPTL3 protein levels and LDL-C in a novel NHP model of HoFH. Key program milestones anticipated in 2022 include:

- Development candidate selection in the second half of 2022, and
- IND-enabling studies to begin in the second half of 2022.

Preclinical Re-Dosing and Sequential Dosing Data

Given the complexities of ASCVD indications, some patients may benefit from additional lipid lowering after treatment with any single agent. Verve conducted multiple preclinical assessments in NHPs to explore the potential to re-dose or sequentially dose its gene editing treatments.

"The best way to treat ASCVD in a patient is to lower circulating LDL-C as much as possible and for as long as possible," said Andrew Bellinger, M.D., Ph.D., chief scientific officer and chief medical officer of Verve. "We've generated preclinical data in NHPs that support our ability to potentially re-dose our PCSK9 base editor. We have also generated data in NHPs that supports our ability to potentially sequentially dose our PCSK9 base editor followed by our ANGPTL3 base editor, which may expand the number of patients who are able to benefit from our therapies. We believe these data are among the first demonstration in NHPs of re-dosing as well as *in vivo* sequential editing of multiple targets and highlight one of the potential key advantages of lipid nanoparticles (LNPs) as a delivery approach for gene editing medicines."

To assess the potential for repeat dosing, Verve conducted a study in NHPs (n=4), in which 0.5 mg/kg of a VERVE-101 precursor was dosed on days 1, 30 and 60 in a 90-day study. Editing of PCSK9 was measured in liver biopsy after each dose on days 14, 46 and 75, and in liver necropsy on day 90. Verve observed an increase in PCSK9 editing over the course of the study, with an average of 29% at day 14, 36% at day 46, 53% at day 75 and 59% at day 90. These data suggest that repeat low doses of a PCSK9 base editor could achieve a high level of liver editing. Importantly, no evidence of liver injury was observed following any of the doses, which provides evidence of the low immunogenicity of LNPs in NHPs.

Patients with very high LDL-C or those with combined hyperlipidemia with high LDL-C and high triglycerides may benefit from gene editing medicines that target two lipid pathways, such as PCSK9 and ANGPTL3. To assess the potential for sequential dosing, Verve conducted a 90-day study in NHPs (n=4), in which 1.0 mg/kg of a VERVE-101 precursor was administered on day 1, followed by administration of 1.0 mg/kg of an ANGPTL3 base editor on day 30. PCSK9 editing was measured by liver biopsy on day 15, showing an average of 71% editing, and ANGPTL3 editing was measured in a second liver biopsy on day 45, showing an average of 52% editing. In liver necropsy on day 90, an average of 69% PCSK9 editing and 63% ANGPTL3 editing was observed. Verve monitored plasma PCSK9 and ANGPTL3 protein levels during the study and observed a greater than 90% reduction of

plasma PCSK9 protein after the first dose and a greater than 90% reduction of plasma ANGPTL3 protein after the second dose, with both reductions remaining durable to the conclusion of the study. These data suggest that sequential dosing of a PCSK9 base editor followed by an ANGPTL3 base editor may be administered to efficiently edit two genes that control key lipid pathways.

Presentation at 40th Annual J.P. Morgan Healthcare Conference

Verve will webcast its corporate presentation from the 40th Annual J.P. Morgan Healthcare Conference on Monday, January 10, 2022, at 4:30 PM ET. A live webcast of the presentation can be accessed under "Events" in the Investors section of the Company's website at vervetx.com. A replay of the webcast will be archived on the Company's website for 60 days following the presentation. In conjunction with the conference, the Company's presentation can be found here: <https://ir.vervetx.com/news-and-events/presentations>.

About Verve Therapeutics

Verve Therapeutics, Inc. (Nasdaq: VERV) is a genetic medicines company pioneering a new approach to the care of cardiovascular disease, transforming treatment from chronic management to single-course gene editing medicines. The company's initial two programs target PCSK9 and ANGPTL3, genes that have been extensively validated as targets for lowering blood lipids such as low-density lipoprotein cholesterol (LDL-C), a root cause of cardiovascular disease. Verve's lead product candidate, VERVE-101, is designed to permanently turn off the PCSK9 gene in the liver in order to disrupt blood PCSK9 protein production and thereby durably reduce blood LDL-C levels, with the goal of reducing a patient's risk for cardiovascular disease. VERVE-101, currently in IND-enabling studies, is being developed initially for the treatment of patients with heterozygous familial hypercholesterolemia, a potentially fatal genetic heart disease. For more information, please visit www.VerveTx.com.

Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the initiation, and timing, of the Company's planned regulatory submissions, future clinical trials, its research and development plans and the potential advantages and therapeutic potential of the Company's programs. All statements, other than statements of historical facts, contained in this press release, including statements regarding the Company's strategy, future operations, future financial position, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the Company's limited operating history; the timing of and the Company's ability to submit applications for, its product candidates; advance its product candidates in clinical trials; initiate and enroll clinical trials on the timeline expected or at all; correctly estimate the potential patient population and/or market for the Company's product candidates; replicate in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials of VERVE-101 and its other product candidates; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; and raise the substantial additional capital needed to achieve its business objectives. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in the Company's most recent filings with the Securities and Exchange Commission and in other filings that the Company makes with the Securities and Exchange Commission in the future. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

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